REMARKS

Claims 21-37 are currently pending. Claims 21-37 are rejected under 35 U.S.C. § 112, first and second paragraph and 35 U.S.C. § 103. The rejected claims have been added to more particularly point out and distinctly claim the invention. No new matter is introduced by the amended claims and the claims are fully supported by the instant specification. For reasons set forth in detail below, Applicants request that the rejections be withdrawn and the claims be allowed to issued.

1. The Claims Are Enabled

Claims 21-37 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleges that while the specification is enabling for a method for identifying a compound capable of modulating polycystin-1 activity by measuring the expression of cell adherence to type I collagen coated substrate, apical expression of NaK-ATPase, or expression of ß-2-NaK-ATPase, the specification does not reasonably provide enablement for a method for identifying a compound capable of modulating mutant polycystin-1 activity.

The test for enablement is whether one reasonably skilled in the art could make and use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. *U.S. v. Telectronics, Inc.* 857 F.2d 778 ??? 8 USPQ 2d 1217 (Fed. Cir. 1988) cert. denied, 490 U.S. 1046 (1989). Furthermore, a patent need not teach, and preferably omits, what is well-known in the art. *Lindermann, Maschinen fabrik GmBH* v. *American Hoist & Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984)..

Applicants assert that the present invention is based on the discovery that cells expressing mutant polycystin-1 protein display a number of mutant phenotypes which include increased adherence to type 1 collagen coated surfaces; apical expression of NaK-ATPase on the cell membrane; increased expression of ß-2-NaK-ATPAse; and decreased focal adhesion kinase (FAK) activity. Moreover, each of the pending claims encompasses methods wherein step(a) of the claimed method requires contacting a test compound to a cell expressing a polycystin 1 protein wherein expression of that protein results in a mutant phenotype.

The instant specification, as filed, discloses that mutant forms of PKD receptor have been identified. The specification further describes (i) methods for assaying cell adherence to type I collagen coated surfaces (p. 23, lines 4-17 of the specification); (ii) methods for assaying expression of NaK-ATPase or the ß2 subunit of NaK-ATPase on the cell membrane (p. 24, lines 3-14 of the specification); and (iii) methods for assaying incorporation of PKD proteins into focal adhesion clusters (p. 25, line 3 through p. 26, line 2 of the specification).

Applicants assert that given the specific teachings of the specification, coupled with knowledge of the structure of the PKD-1 gene as well as mutant forms of the PKD gene, all of which are well established and well-known in the art, one skilled in the art could readily carryout the screening methods of the invention without undue experimentation. The choice of mutant PKD genes and/or cells expressing the specified mutant phenotype is not critical so long as they function for purposes of the subject invention, as described above.

In view of the foregoing remarks and amendments to the claims, the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

2. The Claims as Amended are Definite

Claims 21-37 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleges that the term "over expressed" in Claims 23, 26, 29 and 33 is a relative term which renders the claims indefinite. Applicants have amended the claims to indicate that over expression results in expression of a mutant phenotype.

The Examiner alleges that the term "increase" in Claims 21, 24 and 27 is a relative term which renders the claims indefinite. The Examiner alleges that the term "decrease" in Claim 31 is a relative term which renders the claims indefinite. Applicants have amended the claims to more particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is vague and indefinite because it encompasses a method of identifying a compound capable of modulating any and all polycystin-1 activities, but the method steps would only identify compounds that increase adherence of cells to type-1 collagen.

Claim 24 is vague and indefinite because it encompasses a method of identifying a compound capable of modulating any and all polycystin-1 activities, but the method steps would only identify compounds that increase apical expreesion of NaK-ATPase.

Claim 27 is vague and indefinite because it encompasses a method of identifying a compound capable of modulating any and all polycystin-1 activities, but the method steps would only identify compounds that increase expression of beta2-NAK ATPase.

Claim 31 is vague and indefinite because it encompasses a method of identifying a compound capable of modulating any and all polycystin-1 activities, but the method steps would only identify compounds that decrease focal adhesion complexes.

Applicants have amended the claims to indicate that the method is directed to identification of a compound capable of modulating a specific polycystin-1 activity.

In view of the foregoing remarks and amendments to the claims, the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

3. The Claims Are Not Obvious

Claims 21-31 are rejected under 35 U.S.C.§103(a) as being unpatentable over Wilson et al, (1996) in view of Van Adelsberg. The Examiner alleges that Wilson teaches the correlation between PKD-1 content and degree of adherence to type 1 collagen and Van Adelsberg teaches peptide inhibitors derived from PKD repeats of polycystin 1. According to the Examiner it would have been obvious to one of skill in the art at the time the invention was made to measure adherence of polycystin 1 expressing cells to collagen type-1 in the presence of the inhibitory peptides derived from the PKD repeats of polycystin-1 as taught by Van-Adelsburg, with a reasonable expectation of success. The Examiner maintains that one of skill in the art at the time the invention was made would have been motivated to make this modification to determine if type 1 collagen is a ligand for polycystin-1.

A finding of obviousness under §103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the difference between the

claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S.1 (1996). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 853 F.2d 894, (Fed.Cir. 1988).

In the present instance the relevant inquiry is whether Van Adelsberg in combination with Wilson would render the presently pending claims obvious. Clearly, the answer to that question is no.

Claims 21-31 are directed to methods for identifying modulators of mutant PKD-1 activity. The claimed invention is based on applicants discovery that cells expressing mutant PKD-1 protein display a number of different mutant phenotypes including increased adherence to type 1 collagen coated surfaces; apical expression of NaK-ATPase on the cell membrane; increased expression of ß-2-NaK-ATPAse; and decreased focal adhesion kinase (FAK) activity. Van Adelsburg fails to disclose, or even suggest, a single mutant phenotype associated with expression of mutant PKD-1, much less a screening assay based on a mutant phenotype. Van Adelsburg merely suggest that peptides from the PKD repeats may be used to modulate branching morphogenesis in developing kidney. Further, the deficiency in Van Adelsburg is not supplied by the Wilson reference which fails to disclose, or suggest, screening methods useful for identification of compounds capable of modulating PKD-1 activity.

In light of the above, Applicants respectfully request that the rejections under 35 U.S.C. §103 (a) be withdrawn.

CONCLUSION

Entry of the foregoing remarks into the file of the above-identified application is respectfully requested. The Applicant believes that the invention defined by the amended claims meets all the requirements for patentability. Withdrawal of all rejections and reconsideration of the amended claims is requested. An early allowance is earnestly sought.

Attached hereto as **APPENDIX A** is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Respectfully submitted,

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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

21. (amended) A method for identifying a compound capable of modulating polycystin-1 [activity] mediated increase in cell adherence to type I collagen coated substrate, comprising;

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in an increase in cell adherence to type I collagen coated substrate;

(b) measuring cell adherence to type I collagen coated substrate; and

(c) comparing the level of cell adherence to type I collagen coated substrate obtained in (b) to the level of cell adherence to type I collagen coated substrate obtained in the presence of a vehicle control:

wherein a decrease in the level of cell adherence to type I collagen coated substrate [if the level] obtained in (b) [differs from] compared to that obtained in the presence of a vehicle control, indicates identification of a compound capable of modulating polycystin-1 activity [has been identified].

23. (amended) The method of Claim 21 wherein the polycystin-1 protein is over expressed wherein overexpression of the polycystin-1 protein results in an increase in cell adherence to type I collagen coated substrate.

24. (amended) A method for identifying a compound capable of modulating polycystin-1 [activity] mediated increase in apical expression of NaK-ATPase on the cell membrane, comprising;

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in an increase in apical expression of NaK-ATPase on the cell membrane;

(b) measuring [an increase in] apical expression of NaK-ATPase on the cell membrane; and

(c) comparing the level of [an increase in] apical expression of NaK-ATPase on the cell membrane obtained in (b) to the level of [an increase in] apical expression of NaK-ATPase on the cell membrane obtained in the presence of a vehicle control:

wherein a decrease in the level of apical expression of NaK-ATPase on the cell membrane [if the level] obtained in (b) [differs from that] compared to the level obtained in the presence of a vehicle control, indicates identification of a compound capable of modulating polycystin-1 activity [has been identified].

27. (amended) A method for identifying a compound capable of modulating polycystin-1 [activity] mediated increased expression of ß-2-NaKATPase within the cell, comprising;

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in an increased expression of ß-2-NaKATPase within the cell;

(b) measuring [increased] expression of ß-2-NaKATPase within the

cell; and

(c) comparing the level of [increased] expression of ß-2-NaKATPase within the cell obtained in (b) to the level of [increased] expression of ß-2-NaKATPase within the cell obtained in the presence of a vehicle control:

wherein a decrease in the level of expression of ß-2-NaKATPase within the cell [if the level] obtained in (b) [differs from]as compared to that obtained in the presence of a vehicle control, indicates identification of a compound capable of modulating polycystin-1 activity [has been identified].

29. (amended) The method of Claim 27[,] or 28 [or 29] wherein the polycystin-1 protein is over expressed wherein overexpression of the polycystin-1 protein results in increased expression of ß-2-NaKATPase within the cell.

31. (amended) A method for identifying a compound capable of modulating polycystin-1 [activity] mediated decreased incorporation of focal adhesion kinase into focal adhesion complexes, comprising;

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in a decreased incorporation of focal adhesion kinase into focal adhesion complexes;

(b) measuring [a decreased] incorporation of focal adhesion kinase into focal adhesion complexes; and

(c) comparing the level of [a decreased] incorporation of focal adhesion kinase into focal adhesion complexes obtained in (b) to the level of [a decreased] incorporation of focal adhesion kinase into focal adhesion complexes obtained

in the presence of a vehicle control:

wherein an increase in the level of incorporation of focal adhesion kinase into focal adhesion complexes [if the level] obtained in (b) [differs from] as compared to that obtained in the presence of a vehicle control, indicates identification of a compound capable of modulating polycystin-1 activity has been identified.

33. (amended) The method of Claim 32 wherein the polycystin-1 protein is over expressed wherein overexpression of the polycystin-1 protein results in decreased incorporation of focal adhesion kinase into focal adhesion complexes.